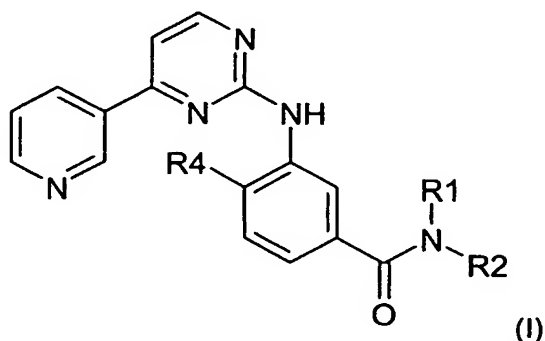


Claims:

1. Use of an inhibitor of one or more protein kinases VEGFR-2, Tie-2, c-Src, c-Met, FGFR-1, Flt-1, HER-2, c-Abl, c-Raf, PDGFR-beta and c-Kit, for the preparation of a medicament for the treatment and/or prevention of neurological and vascular disorders related to beta-amyloid generation and/or aggregation.

2. The use according to claim 1 wherein the inhibitor is a compound of formula I



wherein

R₁ represents hydrogen, lower alkyl, lower alkoxy-lower alkyl, acyloxy-lower alkyl, carboxy-lower alkyl, lower alkoxy-carbonyl-lower alkyl, or phenyl-lower alkyl;

R₂ represents hydrogen, lower alkyl, optionally substituted by one or more identical or different radicals R₃, cycloalkyl, benzocycloalkyl, heterocyclyl, an aryl group, or a mono- or bicyclic heteroaryl group comprising zero, one, two or three ring nitrogen atoms and zero or one oxygen atom and zero or one sulfur atom, which groups in each case are unsubstituted or mono- or polysubstituted;

and R₃ represents hydroxy, lower alkoxy, acyloxy, carboxy, lower alkoxy-carbonyl, carbamoyl, N-mono- or N,N-disubstituted carbamoyl, amino, mono- or disubstituted amino, cycloalkyl, heterocyclyl, an aryl group, or a mono- or bicyclic heteroaryl group comprising zero, one, two or three ring nitrogen atoms and zero or one oxygen atom and zero or one sulfur atom, which groups in each case are unsubstituted or mono- or polysubstituted;

or wherein R₁ and R₂ together represent alkylene with four, five or six carbon atoms optionally mono- or disubstituted by lower alkyl, cycloalkyl, heterocyclyl, phenyl, hydroxy, lower alkoxy, amino, mono- or disubstituted amino, oxo, pyridyl, pyrazinyl or pyrimidinyl;

benzalkylene with four or five carbon atoms; oxaalkylene with one oxygen and three or four carbon atoms; or azaalkylene with one nitrogen and three or four carbon atoms wherein nitrogen is unsubstituted or substituted by lower alkyl, phenyl-lower alkyl, lower alkoxy-carbonyl-lower alkyl, carboxy-lower alkyl, carbamoyl-lower alkyl, N-mono- or N,N-disubstituted carbamoyl-lower alkyl, cycloalkyl, lower alkoxy-carbonyl, carboxy, phenyl, substituted phenyl, pyridinyl, pyrimidinyl, or pyrazinyl;

R₄ represents hydrogen, lower alkyl, or halogen;
or a pharmaceutically acceptable salt thereof.

3. Use according to claim 1 wherein the inhibitor is a compound selected from,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzanilide,
4-Methyl-N-(3-pyridinyl)-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
N-(4-Chlorophenyl)-4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
2(R)- and 2(S)-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzoylamino]propanoic acid,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-N-(8-quinolinyl)benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-N-(3-[trifluoromethoxy]phenyl)benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-N-(2-pyrrolidinoethyl)benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-N-(3-pyrrolidinophenyl)benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-N-(1-[2-pyrimidinyl]-4-piperidinyl)benzamide,
N-(4-Di-[2-methoxyethyl]amino-3-trifluoromethylphenyl)-4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
N-(4-[1H-Imidazolyl]-3-trifluoromethylphenyl)-4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-N-(2-pyrrolidino-5-trifluoromethylphenyl)benzamide,
N-(3,4-difluorophenyl)-4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-N-(3-trifluoromethylbenzyl)benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-N-(3-trifluoromethylphenyl)benzamide,
N-(3-Chloro-5-trifluoromethylphenyl)-4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
N-(4-Dimethylaminobutyl)-4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,

4-Methyl-*N*-[4-(4-methyl-1-piperazinyl)-3-trifluoromethylphenyl]-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[4-(2,2,2-trifluoroethoxy)-3-trifluoromethylphenyl]benzamide,
4-Methyl-*N*-[4-(2-methyl-1H-imidazolyl)-3-trifluoromethylphenyl]-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
4-Methyl-*N*-(4-phenyl-3-trifluoromethylphenyl)-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
4-Methyl-*N*-[4-(4-methyl-1H-imidazolyl)-3-trifluoromethylphenyl]-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
Methyl 2(R)- and 2(S)-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzoylamio]-3-[4-hydroxyphenyl]propanoate,
N-[2-(*N*-Cyclohexyl-*N*-methylaminomethyl)phenyl]-4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
N-[3-[2-(1H-Imidazolyl)ethoxy]phenyl]-4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
4-Methyl-*N*-[3-morpholino-5-trifluoromethylphenyl]-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-(4-pyrrolidino-3-trifluoromethylphenyl)benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-(4-piperidino-3-trifluoromethylphenyl)benzamide,
4-Methyl-*N*-[4-morpholino-3-trifluoromethylphenyl]-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
N-(4-Ethylamino-3-trifluoromethylphenyl)-4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-(3-trifluoromethoxyphenyl)benzamide,
N-[4-(2-Hydroxypropylamino)-3-trifluoromethylphenyl]-4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
N-(4-Diethylamino-3-trifluoromethylphenyl)-4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[3-(3-pyridinyl)-5-trifluorophenyl]benzamide,

N-[3-[3-(1*H*-imidazolyl)propoxy]phenyl]-4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[4-(3-pyridinyl)-3-trifluorophenyl]benzamide,
4-Methyl-*N*-[3-(4-methyl-1-piperazinyl)-5-trifluorophenyl]-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
4-Methyl-*N*-[3-methylcarbamoyl-5-trifluorophenyl]-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide,
4-Methyl-*N*-[3-methylcarbamoyl-5-morpholino]-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]benzamide.
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[3-[3-(1*H*-imidazol-1-yl)propoxy]phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[3-[2-(1*H*-imidazol-1-yl)ethoxy]phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[4-(ethylamino)-3-(trifluoromethyl)phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[4-(diethylamino)-3-(trifluoromethyl)phenyl]benzamide,
(±)-4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[4-[(2-hydroxypropyl)amino]-3-(trifluoromethyl)phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[4-[bis(2-methoxyethyl)amino]-3-(trifluoromethyl)phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[4-(4-methyl-1-piperazinyl)-3-(trifluoromethyl)phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[4-(1-piperidinyl)-3-(trifluoromethyl)phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[4-(1-pyrrolidinyl)-3-(trifluoromethyl)phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[4-(4-morpholinyl)-3-(trifluoromethyl)phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[4-phenyl-3-(trifluoromethyl)phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[3-[4-(3-pyridinyl)-3-(trifluoromethyl)phenyl]methyl]benzamide,

4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[4-(1H-imidazol-1-yl)-3-(trifluoromethyl)phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[4-(2,4-dimethyl-1H-imidazol-1-yl)-3-(trifluoromethyl)phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[4-(4-methyl-1H-imidazol-1-yl)-3-(trifluoromethyl)phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[4-(2-methyl-1H-imidazol-1-yl)-3-(trifluoromethyl)phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[3-(4-morpholinyl)-5-[(methylamino)carbonyl]phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[3-[(methylamino)carbonyl]-5-(trifluoromethyl)phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[5-(3-pyridinyl)-3-(trifluoromethyl)phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[5-(4-morpholinyl)-3-(trifluoromethyl)phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[5-(2-methyl-1H-imidazol-1-yl)-3-(trifluoromethyl)phenyl]benzamide,
4-Methyl-*N*-[3-(4-methyl-imidazol-1-yl)-5-trifluoromethyl-phenyl]-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[5-(5-methyl-1H-imidazol-1-yl)-3-(trifluoromethyl)phenyl]benzamide,
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[3-(4-methyl-1-piperazinyl)-5-(trifluoromethyl)phenyl]benzamide, and
4-Methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[2-(1-pyrrolidinyl)-5-(trifluoromethyl)phenyl]benzamide;
or a pharmaceutically acceptable salt thereof.

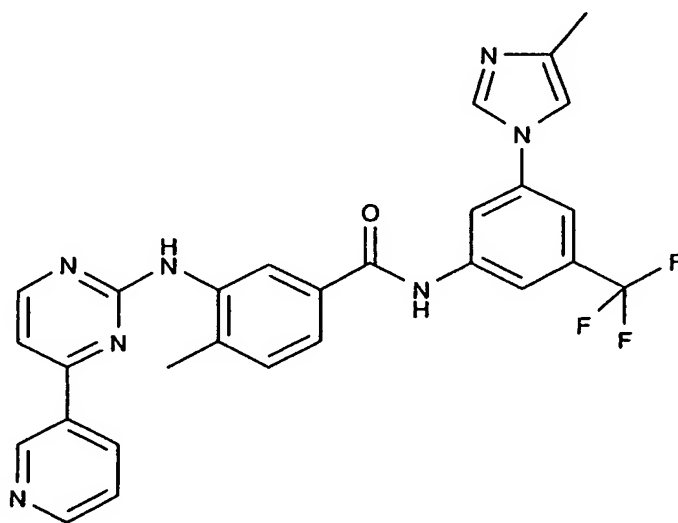
4. Use according to claim 1 wherein the inhibitor is 4-Methyl-*N*-[3-(4-methyl-imidazol-1-yl)-5-trifluoromethyl-phenyl]-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-benzamide;
or a pharmaceutically acceptable salt thereof.

5. Use according to any one of the claims 1-4 wherein a daily dose of 10 to 800 mg of a compound is administered to an adult human.

6. Use according to any one of claims 1 – 5 wherein the disease to be treated is selected from Alzheimer's disease, Down's Syndrome, memory and cognitive impairment, dementia, amyloid neuropathies, brain inflammation, nerve and brain trauma, vascular amyloidosis, or cerebral hemorrhage with amyloidosis.

7. Use according to any one of claims 1 – 5 wherein the disease to be treated is Alzheimer's disease.

8. A method of treating mammals suffering from neurological and vascular disorders related to beta-amyloid generation and/or aggregation which comprises administering to a said mammal in need of such treatment a pharmaceutical composition comprising
(a) a dose, effective against neurological and vascular disorders related to beta-amyloid generation and/or aggregation, of 4-Methyl-N-[3-(4-methyl-imidazol-1-yl)-5-trifluoromethyl-phenyl]-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-benzamide having the formula I

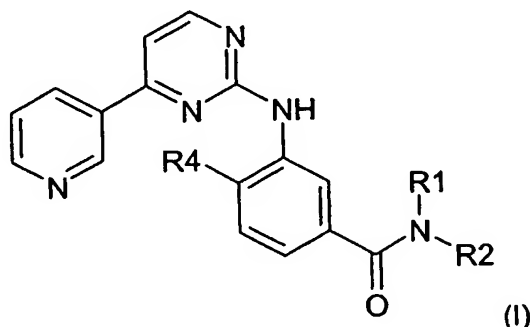


(I);

or a pharmaceutically acceptable salt thereof and

(b) a therapeutically effective amount of a second drug selected from drugs used to treat neurological and vascular disorders related to beta-amyloid generation and/or aggregation.

9. Use of an inhibitor according to any one of claims 1 - 4 or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment and/or prevention of neurological and vascular disorders related to beta-amyloid generation and/or aggregation.
10. A commercial package comprising a compound of formula I



wherein

R₁ represents hydrogen, lower alkyl, lower alkoxy-lower alkyl, acyloxy-lower alkyl, carboxy-lower alkyl, lower alkoxy-carbonyl-lower alkyl, or phenyl-lower alkyl;

R₂ represents hydrogen, lower alkyl, optionally substituted by one or more identical or different radicals R₃, cycloalkyl, benzocycloalkyl, heterocyclyl, an aryl group, or a mono- or bicyclic heteroaryl group comprising zero, one, two or three ring nitrogen atoms and zero or one oxygen atom and zero or one sulfur atom, which groups in each case are unsubstituted or mono- or polysubstituted;

and R₃ represents hydroxy, lower alkoxy, acyloxy, carboxy, lower alkoxy-carbonyl, carbamoyl, N-mono- or N,N-disubstituted carbamoyl, amino, mono- or disubstituted amino, cycloalkyl, heterocyclyl, an aryl group, or a mono- or bicyclic heteroaryl group comprising zero, one, two or three ring nitrogen atoms and zero or one oxygen atom and zero or one sulfur atom, which groups in each case are unsubstituted or mono- or polysubstituted;

or wherein R₁ and R₂ together represent alkylene with four, five or six carbon atoms optionally mono- or disubstituted by lower alkyl, cycloalkyl, heterocyclyl, phenyl, hydroxy, lower alkoxy, amino, mono- or disubstituted amino, oxo, pyridyl, pyrazinyl or pyrimidinyl; benzalkylene with four or five carbon atoms; oxaalkylene with one oxygen and three or four carbon atoms; or azaalkylene with one nitrogen and three or four carbon atoms wherein

nitrogen is unsubstituted or substituted by lower alkyl, phenyl-lower alkyl, lower alkoxy-carbonyl-lower alkyl, carboxy-lower alkyl, carbamoyl-lower alkyl, N-mono- or N,N-disubstituted carbamoyl-lower alkyl, cycloalkyl, lower alkoxy-carbonyl, carboxy, phenyl, substituted phenyl, pyridinyl, pyrimidinyl, or pyrazinyl;

R₄ represents hydrogen, lower alkyl, or halogen;

or a pharmaceutically acceptable salt thereof in the treatment of neurological and vascular disorders related to beta-amyloid generation and/or aggregation, together with instructions for simultaneous, separate or sequential use thereof in the treatment of a proliferative disease.